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Brain activation in Highly Superior Autobiographical Memory:

The role of the precuneus in the autobiographical memory retrieval network

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Abstract

This is the first study to examine functional brain activation in a single case of Highly Superior Autobiographical Memory (HSAM) who shows no sign of OCD. While previous work has documented the existence of HSAM, information about brain areas involved in this exceptional form of memory for personal events relies on structural and resting state connectivity data, with mixed results so far. In this first task-based fMRI study of a normal individual with HSAM, dates were presented as cues and two phases were assessed during memory retrieval, initial access and later elaboration. Results showed that initial access was very fast, did not activate the hippocampus, and involved activation of predominantly posterior visual areas, including the precuneus. These areas typically become active during later stages of elaboration of personal memories rather than during initial access. Elaboration involved a balanced bilateral activation of most of the autobiographical network areas, rather than the more typical shifts observed in people without HSAM. Overall, the pattern of brain activations, which rests on repeated observations in a single individual, highlights a strong involvement of the precuneus and an idiosyncratic initial access to personal memory representations. Implications for the nature of personal memories in HSAM are discussed.

Keywords: Autobiographical memory network; Highly Superior Autobiographical Memory (HSAM); brain imaging; precuneus

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Introduction

Memory for personal events is typically far from perfect. Although people can remember personal events across their lifespan, with a clear increase for young adulthood experiences (reminiscence bump, e.g. Jansari & Parkin, 1996), usually only a handful of events are remembered in detail for each year of life. Two recent single-case reports (Parker et al, 2006; Ally et al, 2013), and four group studies (LePort et al, 2012; LePort, Stark, McGaugh, Stark, 2016; 2017; Santangelo et al, 2018) however, have challenged the limits of autobiographical memory. The case studies (Parker et al, 2006; Ally et al, 2013) described two individuals with the exceptional ability to remember in detail almost every day of their life (Parker et al, 2006; Ally et al, 2013). This rare ability, which has been called either hyperthymesia (Parker et al, 2006) or highly superior autobiographical memory (HSAM), questions the current thinking about autobiographical memory (hereinafter ABM) as being of limited capacity.

The processes responsible for HSAM are still largely unknown, as unknown is whether ABM encoding and retrieval processes in these individuals function in a way similar to the normal population. Data on brain activation can provide valuable information on this issue as the network of areas involved in autobiographical memory in the normal population is relatively well known (e.g McGuire, 2001; Svoboda et al, 2006; Burianova, McIntosh, Grady, 2010). Activation data in individuals with HSAM can reveal the extent to which the same network of brain areas is involved as found in the normal population or whether new areas, typically not part of the autobiographical memory network are also involved. In the present study we examine the brain activation of a new case of HSAM who, differently from the two previously published cases, and the individuals examined in LePort et al (2016; 2017) and Santangelo et al (2018) has no form of pathology. The case described by Ally et al (2013) was an individual who was completely blind from birth, a condition that might have changed encoding processes, and determined the reorganization of a number of brain areas, including those involved in personal memories. Indeed, it is difficult to know which differences in brain structure may be due to blindness and which may be accountable by superior memory. The neuropsychological battery used by Parker et al (2006) in the first reported case revealed the presence of a dysexecutive syndrome, accompanied by a form of Obsessive Compulsive Disorder (OCD). In addition, the woman described by Parker et al (2006) kept a very detailed diary of her entire life, that she constantly rehearsed, which by some has been considered the factor responsible for her exceptional memory (e.g. Marcus, 2009). Consequently, these two case reports offer only limited insight into this exceptional condition.

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A study reporting structural brain data on a group of 11individuals with HSAM (LePort et al, 2012) used four brain imaging methods to compare brain structure in HSAM and controls. Local concentration of grey and white matter in any given voxel throughout the brain was assessed with Voxel Based Morphometry Grey-Matter (VBM-GM) and Voxel Based Morphometry WhiteMatter (VBM-WM); Diffusion Tensor Imaging-Fractional Anisotropy (DTI-FA) assessed differences with controls in white-matter microstructure, while differences in shapes of brain regions were examined using Tensor Based Morphometry (TBM). Results identified nine brain regions that, depending on the type of neuroanatomical analysis used, discriminated HSAM from control in terms of concentration of grey/white matter, shape of the region and white matter tract coherence. These regions include the inferior and middle temporal gyri and temporal pole (BA 20, 21 and 38, respectively), the anterior insula, the parahippocampal gyrus, (BA 36) and the inferior parietal sulcus. White matter tract coherence was also higher in HSAM participants. While these data provide additional insight into potential differences between individuals with HSAM and controls, attributing functional differences to structural differences can be somewhat problematic. As the authors themselves recognize "It is not known of course, whether the anatomical differences observed in our analyses are enabling or resulting from HSAM participants' memory performance." (p.16). They also recognize that some of these anatomical differences might not be linked to HSAM *per se*, rather to OCD, that was observed in more than half of the participants.

Very recently, a study (Santangelo et al, 2018) reported fMRI data on a group of individuals with HSAM and a control group. Participants were presented with cues that referred to the first or the last time a specific event happened, for example "The last time you took a train" or "The first train ride". While memory performance was good among their HSAM participants, their results might be linked to the specific characteristics of the retrieval processes triggered by this type of material. These verbal cues not only refer to specific events in a person's life, they already contain elements of it. These results provide important information on brain areas activated in HSAM individuals while trying to remember these 'first time' and 'last time' specific events. However, what HSAM is characterized by is extensive retrieval of personal memories in response to dates. Five more HSAM individuals tested in our lab, but not reported here, while being superior to the control group also in response to event cues, truly excelled only when responding to dates.

We aimed at addressing some of the concerns and gaps of previous studies by examining in a single-case study a 21 year-old adult, BB, who presented no sign of OCD, autism, or other pathological conditions, who had no physical impairment, and had a normal-to-high level of intelligence. In response to dates, BB was

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able to remember almost every day of his life from approximately age 11. The detailed study of this case, which includes fMRI data, in addition to describing the specific characteristics of this individual, might contribute novel insight into the processes responsible for HSAM. His functional brain activation was assessed against previous group data examining areas that are active in the Autobiographical Memory Network.

The Autobiographical Memory Network

Autobiographical memory is in itself a highly complex system involving a large number of cognitive and non-cognitive components. Cognitive components include episodic and semantic processing (Conway & Pleydell-Pearce, 2000), executive functions (Cabeza& Nyberg, 2000), mental imagery (Ogden, 1993), emotion (Addis, Moscovith et al, 2004) and self-referential processes (e.g. D'Argembeau et al, 2010; Gusnard et al, 2001; Craik et al, 1999).

Major reviews of brain imaging studies of ABM (e.g. Maguire, 2001; Svoboda et al, 2006) have revealed a core network of areas involved in remembering one's personal past. These areas include cortical and subcortical regions in both hemispheres. Maguire (2001), in a review of the first 11 neuroimaging (PET and fMRI) studies of retrieval from ABM, identified a network of predominantly left lateralized cortical areas which included retrosplenial/posterior cingulate cortex, medial temporal regions, the temporoparietal junction, medial prefrontal cortex (Brodmann areas 10,11,9), temporopolar cortex and cerebellum. A more recent meta-analysis of 24 functional studies of ABM retrieval by Svoboda et al (2006) supported Maguire's (2001) earlier findings. These authors also proposed a distinction between a core network of structures activated across most ABM imaging studies (at least in 10 of the 24 studies examined) and two other sets of structures that are less present (secondary regions) or only rarely present (tertiary regions) in the 24 studies. The core network included the medial and lateral temporal cortex, the temporoparietal junction, the medial and lateralretrosplenial/posterior cingulate cortex, the cerebellum, and the ventrolateral prefrontal cortex. Compared to the pattern identified by Maguire (2001), Svoboda et al (2006) observed less involvement of the temporopolar cortex, and a more prominent role for the ventrolateral prefrontal and lateral temporal cortices, which have been thus included by Svoboda et al in the core network. The secondary regions (those activated in at least five of the studies) were areas in the dorsolateral prefrontal cortex (BA 9, 9/46, 46), superior medial and superior lateral cortex (BA 6), anterior cingulate (BA 25, 32, 24), medial orbitofrontal, temporopolar and occipital cortex, thalamus and amygdala. Tertiary regions, found in less than 5 studies, were the frontal eye fields, motor cortex, medial (precuneus) and lateral parietal cortex, fusiform gyrus, superior and inferior lateral temporal cortex, insula, basal ganglia and brainstem.

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While the pattern described above is the typical pattern of brain activation associated with retrieval from ABM in normal individuals who can remember some but certainly not all their past experiences, still little is known, so far, about patterns of activation in individuals with HSAM. Assessing the extent to which areas activated during retrieval in our HSAM case match the core network of areas described by Svoboda et al (2006) in their meta-analysis represents then an important step in understanding this condition.

In this study, functional MRI data were obtained using dates as cues and a novel event-related activation paradigm structured to capture essential differences in the time course of ABM retrieval. The method followed closely the procedure by Daselaar et al, (2008). Brain activity was modelled in two ways, firstly when the memory initially surfaced to mind (initial access), and secondly during elaboration, when the memory was fully formed and detailed. In the average individual, initial access can be relatively fast (<5 sec) in the rare cases of direct retrieval (see Conway & Pleydell-Pearce, 2000), while the process of retrieving a fully detailed autobiographical memory is a relatively lengthy reconstructive process (e.g. Conway, 2005), making it possible to map the time course of changes in brain activation, and differentiate areas contributing to the initial access to a memory from those involved in the subsequent elaboration. Examining brain activation both when memory is accessed and when it is elaborated provides an additional advantage for modelling, as the variability in the time to access a memory represents an inherent ‘‘jitter’’ between the time of the cue and access to the memory (Daselaar et al, 2008). While in the scanner, our participant was asked to indicate when a memory had first surfaced to mind in response to cues. In our case cues were individual dates (e.g. 17th July 2000), as the ability to respond with memories to dates is a specific marker of HSAM. When still in the scanner, our participant was also asked to indicate again when the memory was fully formed and detailed. Daselaar et al (2008) found that initial access (i.e., early stage of retrieval) to individual memories recruited the *right* hippocampus as well as retrosplenial, medial and the *right* prefrontal cortex, whereas visual areas, including the precuneus, and *left* prefrontal cortex showed increase in activation at a later time, during elaboration of individual memories when more details were added (see also Cabeza & St Jacques, 2007). Ours is the first study of task-based brain activation in a single HSAM individual with no sign of OCD, and as such it has mainly an exploratory aim, with the potential to show that OCD is not a necessary trait in determining HSAM.

Method

Participants

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Our HSAM participant, BB, was a healthy male, aged 20 at the time of testing. He was a second-year undergraduate student at a UK University. Informed consent was obtained before starting the study. On some cognitive and neuropsychological tasks, we also tested a control group of 17 individuals of the same age and education level of BB (age range 20-21, 9 females). A control group of 10 adults of the same age and education level was tested in the scanner to obtain structural data. The study was approved by the Ethics Committee of the University of Hull, UK, and the local Ethics Committee at the IRCCS Fondazione Ospedale San Camillo, Venice, Italy, where scanning took place.

Material and Procedure

An overview of the procedure is presented in Figure 1. BB underwent an initial screening with the Hull Memory Screening Questionnaire (De Bartolo et al, 2016), followed by two additional semi-structured interviews. He subsequently completed a large battery of memory tests (some specifically designed for this study, the results of which are reported elsewhere, DeBartolo et al, 2016), and a comprehensive battery of neuropsychological tests.

The Hull Memory Screening Questionnaire contains 20 questions, asking about frequency, content of personal memories starting from the first personal memory up to age 18. In addition, for each event, the participant is asked to report retrieval effort and additional elements about that day. The questionnaire also includes questions referring to events which happened on ten famous dates (e.g. 11/09/2001), questions about the use of a mental calendar and the frequency of use of dates as cues for ABM retrieval. Memory strategies were also investigated, as well as OCD and OCD traits (e.g. keeping a diary, collecting objects etc). Most questions were chosen to cover what previously described as the main characteristics of memory in HSAM (e.g. Parker et al, 2006; CBS documentary, online material).

The main memory battery included visual and verbal long-term and short-term memory tasks from WAIS III and WAIS R; WMS-R; CVLT; REY; Benton. It also included RFM and the AMT (Ivanoiu, Cooper, Shanks & Venneri, 2006), a modification of the AMI (Kopelman, Wilson, & Baddeley, 1990).

Ad hoc memory tests examined episodic memory, episodic autobiographical memory and memory for public events. These included the Autobiographical Dates Test, the main memory test used in this study, in which approximately 500 dates were generated at random, and The Birthday memory test which asked to report what happened on 11 birthdays. The control group was also tested on these tasks (100 dates for the AB Dates test).

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An extensive battery of neuropsychological tests examined a vast array of cognitive functions including executive functions, attention and intelligence (see Table 1). The ones for which there are data from the control group are reported in Table 1.

For the fMRI scanning, two sets of 50 dates were selected three months before the scanning which took place in June 2012, by presenting BB with 288 dates, which covered the previous 15 years (1996-2011 included), and asking him to mark 'Yes' and report the title and a brief description of the memory for that date, if he had any memory, or to mark 'No' if he had no memory for that date. The 50 'Yes' dates were taken randomly from the larger pool of 'Yes' responses, with the constraint that only 5 dates from each given year were included. The second set of 50 dates comprised 'No' dates. Importantly, the consistency of 'Yes' and 'No' dates was verified over several testing occasions, to ensure that the most appropriate testing material would be chosen for the experimental study. During fMRI scanning, 'Yes' and 'No' dates (date/month/year) were randomly intermixed.

Procedure- Screening and Behavioral examination

BB contacted the first author via email, expressing an interest in being tested in response to media advertisements (articles in newspapers, and radio (BBC, UK) interviews) soliciting individuals with an exceptional memory for personal events to contact the first author. He stated that his friends claimed he had an exceptional memory for personal events, although he did not consider his memory really exceptional. Out of 15 individuals who initially responded to the ads, BB was the only one who successfully completed the screening and the two subsequent semi-structured phone interviews on 20 dates chosen at random by the experimenter. The participant was asked to report in detail any memory associated with each specific date. Neuropsychological tests along with the initial battery of memory tests were administered in two separate sessions, held two weeks apart (2 months after the initial screening and one month after the phone interviews). Testing order was scheduled to avoid interference across tests. In addition to several planned breaks, each testing session could be interrupted any time the participant requested to do so. Additional memory testing using 300 out of the 500 initial dates was done over the phone after these two sessions, at different points in time, with intervals ranging between 1 and 3 months between each other, in order to assess test-retest reliability. A subset of the dates (100) was presented on two additional occasions, with a two-month interval between each presentation. Consistency in the reports was assessed by two independent raters, who segmented each report into meaningful units (see Fotopoulou (2005). Consistency could be scored as a 3 (same unit in all three reports), as

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a 2 (present in 2 reports), and 1 (present in one report). Consistency in personal memory reports was also assessed for the day of the week, across two repetitions of 24 dates which were randomly selected from the dates reported as 'remembered' in the scanner.

All tests were administered in person by the second author.

Testing of the control groups followed. Consistency was not assessed. All tests were administered by the first, second and fifth authors.

MRI acquisition, pre-processing and analysis

Brain scanning for this study took place at the IRCCS Fondazione Ospedale San Camillo in Venice, Italy, for both BB and, separately, a control group for structural scanning only. Scanning took place three months after the dates for the scanner were received from BB. Scans were acquired on a 1.5 T Philips Achieva MRI system, fitted with a Sense head coil. The scanning protocol included the acquisition of a T1-weighted structural scan, five functional scans, a T2-weighted axial scan, and a fluid attenuated inversion recovery (FLAIR) scan. To address the experimental question, echo planar single shot T2* weighted MRI images were acquired (TR = 2 s, TE = 50 ms, flip angle = 90°, voxel dimensions 3.28 × 3.28 × 5.00 mm, field of view 230 mm). Two hundred and forty volumes of 20 contiguous axial slices were acquired in ascending order in each run. Each run was preceded by 20 seconds of dummy scans to allow the scanner to reach equilibrium, for a total scanning time of eight minutes and 20 seconds. Five runs were acquired. Total imaging time, including localisation and structural image acquisitions, was approximately fifty-five minutes. In addition, the T1-weighted image was also used to test for the presence of significant volumetric traits. This image was a Turbo Field Echo acquired based on the following specifications: voxel dimensions 1.1 × 1.1 × 0.6 mm, field of view 250 mm, matrix size 256 × 256 × 124, TR = 7.4 ms, TE = 3.4 ms, flip angle = 8°.

Imaging data were analyzed using Statistical Parametric Mapping (SPM) 8 image analysis software (The Wellcome Centre for Human Neuroimaging, London, UK). The T1-weighted image was processed together with the T1 image of 10 male adults of comparable age and educational attainment as BB with normal memory. Images were initially segmented to separate maps of grey and white matter from cerebrospinal fluid. Maps of grey and white matter were normalised based on the SPM 8 anatomical template, and smoothed with an 8 mm full-width at half maximum Gaussian kernel. Functional images were instead slice-time corrected and then all volumes were realigned after creating a mean as reference and re-sliced using 4th Degree B-Spline interpolation methods to adjust for residual motion related signal changes. Volumes were then spatially normalized to the standard EPI template available in SPM 8 using non-linear estimation of parameters. Normalized images were

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then spatially smoothed with a 9 × 9 × 9 mm width at half maximum isotropic Gaussian kernel to compensate for any residual variability after spatial normalization.

Functional MRI paradigm

The fMRI paradigm followed a slow event related design and was an adaptation to HSAM of the procedure used by Daselaar et al (2008). There were two major differences. First, cues were dates rather than words, as in HSAM dates are the most reliable cues for ABM retrieval (Parker et al, 2006). Second, memory events were compared with no memory events and all cues were presented visually. 'No' and 'Yes' dates were presented in random order on a light-grey background and projected via the Nordic Neurolab visual presentation device mounted over the scanner head coil. The experiment started with instructions which were presented for 10 seconds, then stimuli (dates) were presented. After presentation of the date BB had up to 24 seconds to produce his initial response to appearance of memory and then his second response for elaboration. Interstimulus interval was 4 s. BB was instructed to retrieve a memory of a specific event of his life that occurred on that specific date as soon as the cue date appeared on screen. He was asked to press the response button on the Celeritas fiber optic response unit strapped to his wrist, first as soon as the memory was clearly retrieved (access time), but to keep thinking about that memory, as at times additional information would come to mind. He was asked to press the response button a second time (elaboration time) when he felt that the memory was fully formed and complete. For those dates that did not elicit any memories at the time of scanning, BB was instructed to respond by pressing the single response button only once, as soon as he realized that no memory was accessible. All response times were recorded. The content of each memory was collected after scanning took place. The same dates were presented in random order also one week as well as two months after scanning, to assess consistency between the two sets of answers in response to the same dates.

Structural Data Modelling

The comparison between BB's maps of grey and white matter and those of the group of ten young adults was carried out as a modified two-sample *t* test. Age and years of education were added as covariates and both contrasts (BB > controls; controls > BB) were tested. The analyses were thresholded at a set-level uncorrected $p < 0.05$ (further reduced to 0.025 to correct for the number of models: two models, gray and white matter) and only clusters surviving cluster-level Family Wise Error (FWE)-corrected $p < 0.05$ were retained as significant.

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Functional Data Modelling

A general linear model was designed for statistical inference of activation maps. Variability in the BOLD signal within the five runs was modelled as a function of three event-related variables, corresponding to the timepoints when BB pressed the response button. The three events included were as follows: acknowledgment of a date devoid of autobiographical memory, acknowledgment of a date associated with memory access, and acknowledgment of a successful memory elaboration. Events for which a memory access had been acknowledged but no elaboration had been subsequently flagged were discarded.

A synthetic haemodynamic response function (HRF) was used as the reference waveform. Proportional scaling was applied to remove any within subject difference in blood flow. Image data were high-pass filtered with a set of discrete cosine basis functions with a cut-off period of 128 s. Although head motion was less than 2 mm, movement parameters were, however, included as regressors in the analysis. Height threshold was set at $p < 0.05$ FWE-corrected at a set level, to maximise the conservativeness of the outcome. Additionally, a spatial threshold was set at 5 contiguous voxels. The following linear contrasts were tested: recall vs. non-memory, elaboration vs. non memory, recall vs. elaboration, elaboration vs. recall and the conjunct effect of recall vs. non memory and elaboration vs. non memory contrasts. The x, y, z coordinates of significant areas obtained from the analyses were first converted into Talairach coordinates using the Matlab function mni2tal (http://imaging.mrc-cbu.cam.ac.uk/downloads/MNI2tal/mni2tal.m) and then identified using the Talairach Daemon Client (http://www.talairach.org/).

Results

Behavioral results

Autobiographical memory tests. Clear evidence of BB's exceptional ability to remember personal events was found in the tests which examined personal memories triggered by dates. BB was able to report at least one detailed memory for 88.4% of the dates presented. The control group reported an average of 0.03% memories for the dates presented. In the few instances in which controls could retrieve a memory in response to dates, retrieval time was 11.52 sec. In BB, consistency analysis showed that the same day of the week was reported on 92% of the dates across repetitions. Of all 657 units of content examined in the 100 memories tested several times, 618 (94%) received a consistency score of 3, 30 (5%) a score of 2 and 9 (<1%) a score of 1.

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Additionally, the reality of factual elements reported in the autobiographical memories elicited by the dates (e.g. the names of shops and commercial venues, television programs and their contents, the weather on that specific date) was assessed with multiple means. In BB accuracy was 98%.

For the Birthday memory test, BB had no recall of the first two birthdays, but was able to report detailed memories for all the remaining birthdays. Memories for a subset of birthdays (5) was assessed a second time, and accuracy was 100%. The control group remembered an average of 2.6 birthdays.

Phenomenological characteristics of the memories. Retrieval time in response to dates was very fast (1.8 sec in average). Only for a minority of dates, BB needed to think for more than a few seconds. And only in two cases he needed to spend more than 20 sec to come up with a memory. These latter instances resulted in vague reports, with minimal or almost no details. But in most of these cases he could afterwards swiftly report complete events that happened on a day close to that date. For retrieved memories, he commented that they 'popped-up' as a date was mentioned, effortlessly, in a visual and very vivid form. Some details, mostly visual, were already present in the initial memory, and he stated he could 'see' more details by 'zooming into the memory'. Weather conditions, people and locations were present during access. The process of 'zooming in' not only allowed him to 'see' more details for that day, but also to move forwards and backwards in time, and 'see' days nearby, which could be in turn also 'zoomed-in' to see their respective details. His reports evidence the visual nature of his memories, and the presence of somatosensory information, whereas other senses (smell, taste) seemed to be of lesser importance. A strong sense of recollection accompanied all the complete memories reported. He was also able to state the exact day of the week for nearly every date mentioned, and he claimed that the day of the week 'came' with the date. This, however, seemed more the result of a perfected practice (as in some savants, e.g. De Marco, Iavarone, Santoro, Carlomagno, 2016), since he was able to explain the pattern of date-to-day correspondence across the years, and tell the day of the week for dates that preceded his exceptional memory as well as future dates.

Neuropsychological tests

*Intelligence***.** The results of all neuropsychological tests are reported in Table 1. BB's IQ was above the norm, in the top 90th percentile. He achieved top scores in object assembly, block design, picture completion tests (WAIS-III performance), and in the Symbol Search task (scaled score 19 out of max 19). Performance was above average (12/19) in Information and Letter-Number sequencing, while it was average for Picture Arrangement (50th percentile) and low (25th percentile) in the Digit Symbol task.

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Standardized memory tests. BB achieved top scores in the Figural Memory task (WMS-R), in the Long Delay Yes-No Recognition and the Long Delay Forced Recognition tasks of the CVLTII. His scores were within the 99th percentile on both immediate and delayed Visual Reproduction (WMS-R) and verbal working memory tasks (forward digit span, WMS-R). They were in the top 90th percentile for the verbal backward digit span and the visual forward span (WMS-R). Performance was above average both in the Copy (36/36) of the REY figure and in the Rey memory task (27/36) and in the Benton test (recognition of unknown faces, 88-97th percentile). However, scores were only in the 78th percentile in the visual backward span (WMS-R), and in the 73rd and 66th percentile respectively on the WMS-R Logical Memory I and II tasks. Notably, BB's performance was average in most tasks of the CVLT-II, in which his recall scores were between the 50% and 75% of the highest possible score, with an average of 61.25% (see Table 1).

Executive tasks. Performance was very high in many executive tasks (top score in Mental Control, no errors in the Trail Making and Stroop tasks). However, overall performance on the Stroop task was average. His score on the Trail Making test fell within the 90th percentile, both for tests A and B, and scored slightly above average in the D-KEFS tests. In general speed was very high in most tasks.

Linguistic abilities. The score on the WAIS-R comprehension test was within the 84th percentile, and the scaled score for the Vocabulary test was 16 (out of a maximum of 19). He scored high in the D-KEFS Verbal Fluency task (14/19 and 19/19), but average on the Boston Naming test (50th percentile).

fMRI Scanning

Behavioral results. BB reported a memory for forty three of the fifty dates for which three months earlier he had been able to retrieve a memory ('Yes' dates). He also unexpectedly reported a memory for fifteen of the fifty dates for which three months earlier he could not ('No' dates). The average time to retrieve a memory was 1816msec (sd = 1305msec) for the 'Yes' dates, and 1952msec (sd = 1253msec) for the fifteen memories for 'No' dates. Time to respond 'no' (no memory) to a date was 2981msec (sd = 3215msec) for 'No' dates, and 7633msec (sd = 1303msec) for 'Yes' dates for which no memory was retrieved. This latter difference can be explained as due to searching unsuccessfully for the memory for dates that felt familiar. The average time to

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obtain a complete memory (elaboration) was 11725msec (sd=3750msec) for memories retrieved in response to 'Yes' dates and 16196msec (sd = 3694msec) for memories elicited by 'No' dates.

The concordance between raters about the consistency in the content of these memories was very high (99%), overall. Out of 590 units, 570 (or 96.6%) received a score of 2, 12 (or 2%) a score of 1 and 8 (1.4%) a score of zero. Consistency was very high in both sets of memories. Four hundred and forty (or 98%) of the 'Yes' dates (449) received a score of 2; 6 (1.3%) a score of 1 and 3 (<1%) a score of zero. Of 'No' dates (141), 134 (95%) received a score of 2, 4 (3%) a score of 1, and 3 (2%) a score of zero.

Functional activation data

fMRI events were determined by BB's response times both for 'Yes' and 'No' dates. Results are reported separately for initial access and for elaboration, comparing memory to no memory events. Access and elaboration were also directly contrasted. Table 2 lists regions recruited during memory access and elaboration. All major findings are illustrated in Figure 2A-C.

Memory access: Activation was observed primarily in the cerebellum, bilaterally, as well as in left posterior visual association areas (mainly the precuneus and the cuneus). Significant activation was also seen bilaterally in associative occipital areas (BA 18 and 19), and ventrolateral prefrontal areas (right: BA 45 and 47; left: BA 11 and 46). Additional activation was observed in the left amygdala, the temporoparietal junction and the posterior cingulate. Activation was also present in the left parahippocampus, only when a less stringent significance threshold was used ($p<.001$ uncorrected).

Memory elaboration: Activation was observed primarily in the temporo-parietal junction (areas 39 and 40) bilaterally, and prefrontal areas, also bilaterally (mainly BA 9, 10, 11, 46 and 47). Activation was also observed in visual areas (precuneus and occipital areas) bilaterally, as well as in temporal areas and the cerebellum, again bilaterally. The left parahippocampus and amygdala were not active in this phase.

Access vs elaboration. A direct comparison of access and elaboration revealed a marginally greater activation during access in left areas, and a greater engagement of occipital visual regions, mainly the left lingual gyrus and the right cuneus, plus bilaterally the precuneus (left PC: -8 -70 37; right PC: 40 -76 39). Greater activation in access than in elaboration was also observed in prefrontal areas (BA areas 9 and 6) bilaterally, as well as in the right posterior cingulate and in the cerebellum.

Elaboration vs access. Elaboration showed a bilateral pattern of activation across a larger number of areas, with greater recruitment primarily in temporal areas (BA 39 and 22), but also in parietal (including, but

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not limited to the precuneus, right PC: 4 -70 44; left PC: 0 -65 25) and in a large number of prefrontal areas (BA 4,6, 8, 9,10,11,46 and 47). Activation was also observed in the anterior cingulate bilaterally, right insula, right cingulate, right claustrum.

Conjunction analysis revealed that the areas in common to the two phases of retrieval were located in the left hemisphere, with the exception of the right middle temporal gyrus in the occipital lobe (BA 19). They included foremost the precuneus, as well as visual (BA 19), temporal (BA 38 and 39), frontal (BA 11, 46, 47) regions, the cingulate gyrus and the cerebellum.

Anatomical Variables

All anatomical images of the MRI protocol were reviewed by a senior neuroradiologist, who recognised no abnormalities. BB had significantly larger grey-matter volumes in a large left occipito-temporal cluster which extended to the posterior hippocampus (Figure 2D; Table 3). No significant clusters were found for the opposite contrast. No significant white-matter differences beween BB and the control sample were found.

Discussion

The behavioural data obtained in BB confirm that his is a clear case of HSAM, with no form of cognitive impairment and the ability to retrieve almost every day of his life starting from age11. His performance on the various autobiographical memory tasks was extremely high, with a fast retrieval and high levels of test-retest consistency in his personal memory reports (which indicates that these were not made-up confabulations). Personal memories were mainly reported as being visual. BB reported to be able to 'see' almost automatically and effortlessly the events when presented with the cueing dates, and to be able to visually zoom into the scene, expanding it back and forth in 'time', and scanning and 'seeing' clearly its visual details. Interestingly, no sign of OCD or autism were observed, which shows that individuals with HSAM are not necessarily affected by OCD traits as claimed elsewhere (e.g. Marcus, 2009). More recently, both LePort et al (2016) and Santangelo et al (2018) also reported significantly higher OCD scores in their HSAM groups compared to controls. It is likely that an OCD tendency contributes towards using specific strategies (e.g. keeping a diary, reading the diary) and compulsory rehearsal, which in turns helps remembering details and have a better memory. However, the lack of OCD tendencies in BB indicates that neither OCD nor compulsory rehearsal are essential factors in determining HSAM.

Differently from his performance for personal memories, BB's performance on other episodic memory tests ranged from average, for verbal episodic memory, to above average for some visual memory tasks, a result

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that is in agreement with recent data (LePort et al, 2017), also showing that in HSAM, performance in non-personal memory tasks is average. Although the screening procedure adopted by the authors was somewhat different from ours, both their HSAM participants and BB did not differ substantially from the control group in a various array of cognitive skills, while differing substantially in their ability to remember personal events.

Behavioral results while in the scanner

Access and retrievability of each memory was variable, as in most individuals. Variability might have been triggered by the fast pace of presentation of the dates, potentially penalizing memories that were slower to access. It might also be due to random and transient facilitated or hindered access to memories. These potential explanations cannot be addressed with the current data.

It is interesting to note that the average response time for initial access to memories was very short, much shorter than in previous studies (e.g. Daselaar et al, 2008). BB's fast retrieval cannot be solely attributed to the fact that the same dates (among many others) had been already presented. The presentation interval was three months and too many dates were presented to remember them all, given also BB's average performance in episodic memory tasks. Very fast access times speak instead in favour of a facilitated access to personal memories (to anticipate data not reported here from another five individuals with HSAM who have been more recently examined, the same very fast access to memory was found in all of them). Previous work had shown that retrieval is faster for repeated (more semanticized) autobiographical memories (e.g. Addis McIntosh, Moscovitch, et al., 2004), while more specific autobiographical memories are characterized by longer retrieval times (e.g. Graham et al., 2003). While this difference suggests that also in the normal population semanticized autobiographical memories might represent the preferred level of access (see also Conway & Pleydell–Pearce, 2000), here it is important to remark that in BB fast-accessed memories have <u>*all*</u> the qualities of unique, highly specific events, and do not resemble semantic, repeated or scripted memories.

Retrieval time for memory elaboration was relatively long, in line with previous results for memory access (Daselaar et al, 2008), and different between elaboration of 'Yes' (faster) and 'No' (slower) dates. Parsimoniously one can explain this difference by assuming that details of memories for 'No' dates were in general less accessible, or based on weaker or less structured traces, as a few months before BB was not able to access these memories at all. The alternative explanation (they were just confabulations) can be ruled out considering the high content consistency across re-testing sessions, which was not different for 'Yes' and 'No' memories.

Functional activation

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There are five main findings. First, differently from prior studies on the retrieval from autobiographical memory, in BB there was extensive activation of visual areas already during memory access. Second, while access triggered left areas, elaboration was characterized by a more balanced bilateral activation, whereas previous findings (e.g. Daselaar et al,2008) observed a predominantly right activation. Third, self-reference areas such as the MPFC (e.g. D'Argembeau et al, 2007) were not involved while areas more rarely found to be activated during ABM retrieval were instead highly active. Fourth, the typical anterior-to-posterior pattern of activation observed in previous studies on autobiographical retrieval (Conway, Pleydell-Pearce, & Whitecross, 2001; Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2003) was missing, with a more balanced involvement of both anterior and posterior regions. Fifth, overall retrieval, and in particular during elaboration, involved most of the areas of the autobiographical network already observed in previous reviews (e.g. McGuire, 2001; Svoboda et al, 2006).

Access

During *access*, both in the access vs no memory contrast and the contrast between access and elaboration, the major difference between BB's data and previous results (e.g. Svoboda et al, 2006; Daselaar et al 2008) is in the strong activation of the precuneus, that has been previously linked to visual imagery and to the retrieval of true memories in normal individuals (e.g. Addis, McIntosh, Moscovitch, et al. 2004). Activation was bilateral, although predominantly left. The precuneus is a tertiary area in the Svoboda et al (2006) meta-analysis, but one of the most active in BB.

Functional imaging studies have involved the precuneus in a diverse array of highly integrated functions (Cavanna & Trimble, 2006), including visual memory (Fletcher et al, 1996: Gardini et al, 2005; Gardini et al, 2006, see also the role in correct recognition of presented items, Rugg, 1995). More recently it has been linked to recollective processes (being able to re-live the event) in episodic recognition (Dobbins & Wagner, 2005; Henson, et al. 1999; Wheeler & Buckner, 2004). In normal individuals, the left (and to a lesser extent right) precuneus is also associated with the specificity of personal information retrieved (Addis, Moscovitch et al., 2004-1; Addis, McIntosh, Moscovitch et al. 2004). Some have also shown the involvement of this brain area in self-processing operations (first-person perspective taking and experience of agency, Cavanna & Trimble, 2006), and in the complex network of neural correlates of self-consciousness (e.g., self-related mental representations during rest), which are part of the retrieval of personal memories. Both visual and self-referential roles might contribute to explain the unusual strong, predominant activation of the precuneus

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during access in BB. Other visual associative areas were also highly active during access, which have been considered secondary areas in the ABM network, supporting the strong visual component of BB's personal memories.

Other areas active during access are part of the core areas in the autobiographical memory network (cerebellum, retrosplenial/posterior cingulate, temporo-parietal junction). Secondary areas included, in addition to the occipital lobe, DLPFC, orbital FC, cingulate gyrus and temporal pole. In addition to the left precuneus, during access activation was observed in the left VLPFC, which is involved not only in memory search and controlled retrieval (Badre et al, 2005; Badre & Wagner, 2007), but, more importantly for our results, reflects the contribution of semantic information to autobiographical memory (Cabeza & St Jaques, 2007).

Overall during access there is a strong left activation. Although contradicted by clinical neuropsychology data (e.g. Kopelman & Kapur 2001) which tend to implicate right frontal areas, this strong left activation is not uncommon in studies of retrieval from autobiographical memory (Conway et al., 1999; Maguire and Mummery, 1999; Maguire et al., 2000, 2001; Maguire and Frith, 2003; Piefke et al., 2003). It has been variously explained as being due to paradigms which rely on verbal cues and verbal recall when testing ABM (Svoboda et al, 2006), to the retrieval of memories already retrieved shortly before scanning (Daselaar et al, 2008), or to a quick, intuitive, preconscious (Moscovitch & Winocour, 2002) post-retrieval monitoring, a 'feeling of rightness' referring to the veridicity and cohesiveness of retrieved memories in relation to an activated self-schema (Gilboa, 2004). Given the procedure, involving the presentation of dates and the large (3 month) interval between trial repetition, only the monitoring hypothesis might apply for our results.

The predominant left lateralization observed in this case might however lead to a different interpretation when considered in conjunction with BB's very fast retrieval times, the very high consistency across repetitions and the strong involvement of visual areas already during access. The left VPFC indicates the contribution of semantic memory in ABM. Fast access typically indicates direct retrieval (e.g. Uzer & Brown, 2012), which does not involve top-down hierarchical reconstructive processes. It has also been interpreted as an initial 'check' of semanticized, factual LTM, in an otherwise slower retrieval (e.g. Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2002). The early activation of visual areas show the strongly visual nature of personal memories in BB. Considered together, the results on access (vs no memory as well as vs elaboration) might then suggest that in BB personal experiences are retrieved as factual, readily accessible, knowledge (similar to math facts, 2x2=4), rather than genuine episodic memories which typically are the outcome of a longer reconstructive

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processes (Conway & Pleydell-Pearce, 2000). If so, this pattern of results can indicate an idiosyncratic semanticized or fact-like representation of personal memories. This is in line with the hypothesis proposed by LePort et al (2016) for HSAM memory superiority. The authors compared details of memory reports about personal events in HSAM and controls at different time intervals. No difference was found in immediate recall, while difference increased over time, suggesting that superior memory might be attributed to a rather unique consolidation process. Our results not only are in agreement with this hypothesis, they might also complement it by providing some initial evidence suggesting that the difference in consolidation could be attributed to a progressive strongly visual 'factualization' (e.g. as math facts are in some individuals) of personal memories. In terms of retrieval processes, turning personal memories into facts facilitates a direct access to the representation, avoiding the reconstructive processes typical of retrieval of personal memories in the normal population (see for example the hierarchical model proposed by Conway & Pleydell-Pearce, 2000).

Interestingly, and differently from Daselaar et al (2008), and Santangelo et al, (2018), we found no hippocampal activation during access. It is well established that the hippocampus is involved in episodic memory consolidation and retrieval (e.g. Addis, Moscovitch et al, 2004), and this result might seem at first surprising. However, it should be noted that in both Daselaar et al (2008)-normal individuals-, and Santangelo et al (2018) -HSAM-, the task was to report memories in response to truly episodic, event-related, cues. For example, Santangelo et al (2018) cued the memories with requests like 'The first time you drove a car' and 'The last time you took a train'. These cues contain already parts of the episode and might require a retrieval process which is different from the one activated by dates, which were used with BB. Hippocampal activation in Santangelo et al's (2018) HSAM might be due to the nature of the retrieval, which is intentional and most likely generative and effortful (Conway & Loveday, 2010), accessing specific episodes, whose content is already suggested in the cues. In the case of BB, instead, no episodic content was provided, and while certainly intentional, retrieval was subjectively perceived as direct and effortless when successful. In addition, our cues were dates. To our knowledge ours is the first study using dates as cues, and further studies should examine if dates might trigger different retrieval processes that bypass the hippocampus.

While the role of the hippocampus in retrieving episodic memories from dates needs to be further examined, the lack of hippocampal activation observed in BB could support the interpretation proposed above for the other results (retrieval speed, consistent left frontal activation, activation of visual areas during access), which all potentially point to the special nature of the representation of these memories, as somewhat 'pre-packaged', factual, visual, and apparently retrieved differently from other episodic memories in the same

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individual. We would like to remind that BB performance in other episodic memory tasks was average. It would be interesting to examine hippocampal activation in very fast direct retrieval also in non HSAM individuals.

Elaboration

Differently from access, during *elaboration*, when contrasted with no memory, almost *all* areas of the core network were recruited, and, differently from the results in the normal population, in BB activation was *mostly bilateral*. Core network areas were active as well as secondary and tertiary areas in the Svoboda et al, (2006) review. We should note that the precuneus was active also during elaboration. The Elaboration vs Access contrast confirms engagement of MTL, prefrontal areas and, bilaterally, the anterior cingulate cortex. In sum, elaboration engaged all areas found in the 24 studies reviewed by Svoboda et al (2006), with the exception of the anterior cingulate, brain stem and basal ganglia.

The bilateral activation observed in BB during elaboration has never been observed before in ABM retrieval. BB's activation does not show any clear left-to-right shift over the course of retrieval (between access and elaboration), as left areas remain consistently activated during the whole course of remembering while previous electrophysiological studies indicate a shift from left to right hemispheric engagement over the course of remembering (Conway, Pleydell-Pearce, &Whitecross, 2001; Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2003). Differences from previous findings were also observed in the timeline of activation in BB's data. Previous work using electrophysiological data suggests that retrieval from ABM seems to follow a general anterior-to-posterior trend, showing that during retrieval and maintenance of ABMs a shift occurs in cortical potentials from predominantly left frontal regions to posterior temporal and occipital regions (Conway et al. 2001, 2003). The frontal-to-posterior trend has also been confirmed in fMRI by Daselaar et al (2008), with engagement in right PFC regions during initial access of ABMs, followed by activation in the visual cortex and the precuneus during elaboration. The pattern observed in BB was instead almost the opposite. Although, as in previous studies, during initial access to personal events some frontal areas were also recruited (mainly left (5) but also right (3)), activation of posterior areas was predominant, reinforcing the observation about the role of visual access to memories in HSAM. Conversely, elaboration engaged posterior and anterior areas, bilaterally in equal manner.

During this phase, brain areas involved in self-referential processes were also engaged (medial PFC, D'Argembeau et al, 2007), suggesting that elements connected to the self and to more episodic elements might become more active when elaborating the material provided by the initial access.

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Structural data revealing larger grey-matter volume in a left posterior cluster also confirm the major role of visual areas in BB.

Overall, the results on access and elaboration, when compared to no memory, suggest that in BB retrieval from Autobiographical memory might be organized in terms of a very effective interplay between initial highly accessible factual and visual autobiographical representations, followed by the retrieval of additional details of the event that can be more episodic and self-referential in nature. Curiously this picture corresponds rather closely to the subjective self-report of BB about his mental processes during retrieval, when he describes how hearing a date would immediately and effortlessly reveal a picture that contained some initial basic elements and events of the day. This would be followed by the possibility of zooming in (still in a visual modality), and 'see' the day with its more specific elements (activities, locations, objects, people, conversation) that are displayed almost as if in a movie.

Conclusions

The results of the functional brain imaging procedure in BB reveal an overall pattern that seems to be rather specific to this case, but might also be common to other individuals with HSAM. It is almost the opposite of that observed in individuals who don't possess an exceptional personal memory. A larger grey matter in posterior areas, as well as a predominantly posterior activation already during access reinforce the observation about the highly predominant role of visual areas during the retrieval of personal memories. During elaboration both hemispheres are simultaneously involved, both anteriorly and posteriorly, revealing a somewhat balanced bilateral activation. Finally, the remarkable speed of access to the memories (less than 2 sec on average) suggests that access to personal memories, in response to dates, most likely depends on direct retrieval, which is facilitated by the visual component. There is a substantial overlap between brain areas activated during retrieval of personal information in response to dates and areas which are part of the core autobiographical memory network. Responding to dates, however, seems to show a more efficient, and somewhat different, processing of information. This conclusion is in line with the interpretation of relatively recent structural data (Le Port et al, 2012) documenting structural differences in a sample of individuals with HSAM compared to a control group, differences which pertain to many of the core network areas, leading the authors to suggest a more efficient use in HSAM of the same autobiographical memory 'hardware'. We would add that left-posterior areas in BB have more grey matter.

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While it is tempting to consider the pattern of brain activation observed in BB as predictor of HSAM, it remains necessary to consider these results with caution. Typically, there is substantial variability across normal subjects in terms of the regions activated and the strength of activation during autobiographical memory retrieval. To date, the extent of such variability remains rather unknown, as there is no data set using the same task to provide standardized activation scores. This implies that the observed pattern and its deviation from other group level findings cannot per se fully explain the mechanism underlying HSAM. Nonetheless, the descriptive results of retrieval and brain activation pattern obtained in BB, as well as their interesting correspondence with his subjective report on his retrieval experience, can provide additional information that can spark new insight into the processes involved in highly superior autobiographical memory.

Compliance with Ethical Standards:

None of the authors has a conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Pre-registration: No part of the study procedures and analyses was pre-registered prior to the research being conducted.

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TABLES

Table 1. Main neuropsychological tests results. Standardized scores represent percentiles.

Table 2. List of brain regions activated during access and elaboration

Table 3. Significant volumetric differences of gray matter between BB and a group of 10 young males of comparable age and educational attainment.

FIGURES

Figure 1

Flow chart illustrating the procedure

Figure 2

Graphic depiction of the main findings of the study. A) Pattern of activation associated with date-related recall. Whenever BB recognised that a date was specifically associated with a memory, activation was seen in a set of regions including, as depicted by these slices, the precuneus, ventromedial prefrontal cortex, amygdala and various occipital areas. Slice in the Montreal Neurological Institute (MNI) space are as follows: x = -19, y = -9, z = 0, x = -3. B) Pattern of activation associated with elaboration of memories. When specific recalled memories were then further processed in terms of content, extensive activation was seen in temporal, parietal, prefrontal and occipital regions, without any significant contribution offered by mediotemporal regions. Slice in the MNI space are as follows: x = -52, y = -9, z = 6, x = -3. C) Conjunction analysis showing the spatial intersection between recall and elaboration in the precuneus and in the temporo-occipital territory, bilaterally. MNI slices are as follows: z = 9, x = 3. D) Regions in which BB had more volume than the group of normal young male controls. These are only grey matter, and were found in the left occipital and temporal lobe, extending to the posterior part of the hippocampus. MNI slices are as follows: x = -32, z = 10. All images are in neurological visualization. All results are expressed as *z* scores (color coding proportional to the size of *z* scores is shown on the right hand-side of each map).

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Table 1. Cognitive and neuropsychological assessment. Comparison with controls was performed only for non-standardized tests.

Tasks	**BB**	**Controls**	**sig.**
Autobiographical Memory			
Dates %	88.4	0.03	*p<.001*
Retrieval time (sec)	1.8	11.52	*p<.001*
Birthdays	9	2.06	*p<.001*
Memory			
Verbatim memory text	12*	3.71	*p<.001*
Rey figure copy	29	35.22	*n.s.*
Rey figure memory	23*	12.13	*p<.001*
Paired associates visual	30*	18.41	*p<.01*
Recognition scrambled dates	5*	0	
Memory date-event	3	1	*n.s.*
Episodic memory correct	27	26	*n.s.*
Face recognition (RTM)	0.83	0.77	*n.s.*
Attention			
Stop-Signal	269.4*	339	*p<.01*
Negative priming	6.3*	29.9	*P<.01*
Stroop errors	0	0	*n.s.*
Stroop time	15.39	10.02	*n.s.*
Other tasks	**Standardized scores**		
Verbal fluency Letters	17	NA	
Verbal fluency Category	28	NA	
WRAT spelling	87	NA	
WRAT arithmetic	75	NA	
WAIS arithmetic	84	NA	
WAIS comprehension	50	NA	
WAIS picture arrangement	100	NA	
WAIS object assembly	100	NA	
WAIS picture completion	99	NA	
WAIS digit symbol	25	NA	
WAIS III symbol search	19 scaled score	NA	
WAIS III vocabulary	15 scaled score	NA	
Edinburgh handedness	R:17 L:3	NA	
WMS-Logical	70	NA	
WMS-Visual reproduction	99	NA	
CVLTII Free recall repeated	62	NA	
CVLTII Free recall immediate	65	NA	
CVLTII Free recall short del	75	NA	
CVLTII Cued recall short del	50	NA	
CVLTII Free recall long del	65	NA	
CVLTII Cued recall long del	50	NA	
CVLTII Recog long del	100	NA	
CVLTII Forced recog long del	100	NA	

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Table 2A. Significant differences in activation comparisons in Access vs. No Memory (top) and Elaboration vs. No Memory (bottom). The areas with the highest differences in activation (z score >5.5) are reported. Analyses were computed an all significant areas.

Access vs. No Memory

Cluster Number	Cluster-level pFWE	Cluster Extent (voxels)	Region	Local Z-Score	BA	Side	Talairach Coordinates		
							x	y	z
1	< 0.001	120	Cerebellum – Culmen	7.21		L	-8	-54	-1
			Cerebellum – Culmen	5.88		L	-8	-43	-5
2	< 0.001	70	Middle Frontal Gyrus	6.71	11	L	-32	34	-19
3	< 0.001	54	Cerebellum – Tuber	6.63		L	-42	-69	-23
4	< 0.001	109	Precuneus	6.51	7	L	-2	-56	53
			Superior Parietal Lobule	5.94	7	L	-8	-67	59
			Precuneus	5.07	7	L	-10	-75	53
5	< 0.001	85	Lingual Gyrus	6.31	18	L	-20	-56	3
6	< 0.001	106	Precuneus	6.31	19	L	-34	-78	33
			Precuneus	5.67	19	L	-30	-82	39

Elaboration vs. No Memory

Cluster Number	Cluster-level pFWE	Cluster Extent (voxels)	Region	Local Z-Score	BA	Side	Talairach Coordinates		
							x	y	z
1	< 0.001	1866	Middle Temporal Gyrus	Inf.	39	L	-48	-75	9
			Middle Temporal Gyrus	Inf.	39	L	-36	-55	23
			Inferior Parietal Lobule	Inf.	40	L	-44	-54	56
2	< 0.001	1087	Superior Temporal Gyrus	Inf.	22	L	-51	13	-6
			Inferior Frontal Gyrus	Inf.	47	L	-48	40	-7
			Superior Frontal Gyrus	7.38	10	L	-34	57	12

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3	< 0.001	210	Middle Frontal Gyrus	Inf.	11	L	-34	58	-13
4	< 0.001	1303	Middle Temporal Gyrus	7.79	39	R	48	-68	9
			Superior Temporal Gyrus	7.71	22	R	61	-54	10
			Superior Temporal Gyrus	7.67	39	R	53	-52	10
5	< 0.001	1161	Precuneus	7.66	7	R	2	-70	44
			Precuneus	7.61	7	R	2	-58	38
			Posterior Cingulate Gyrus	7.58	23	L	-4	-57	19

Table 2 B. Significant differences in activation comparing Access and Elaboration

Access vs. Elaboration

Cluster Number	Cluster-level pFWE	Cluster Extent (voxels)	Region	Local Z-Score	BA	Side	Talairach Coordinates		
							x	y	z
1	< 0.001	167	Lingual Gyrus	Inf.	18	L	-28	-97	-4
			Lingual Gyrus	7.10	17	L	-16	-99	-8
2	< 0.001	46	Precuneus	7.43	7	L	-8	-70	37
3	< 0.001	183	Middle Frontal Gyrus	7.32	9	L	-50	13	34
			Precentral Gyrus	6.61	9	L	-32	6	33
			Precentral Gyrus	6.12	9	L	-40	6	37
4	< 0.001	255	Cerebellum - Culmen	7.17		R	10	-51	-3
			Cuneus	6.76	30	R	12	-58	8
			Posterior Cingulate Gyrus	6.46	30	R	20	-56	12
5	< 0.001	43	Cuneus	6.81	19	R	8	-80	35
6	< 0.001	115	Medial Frontal Gyrus	6.69	6	L	-2	12	47
7	< 0.001	38	Fusiform Gyrus	6.68	37	L	-48	-59	-12
8	< 0.001	83	Cerebellum - Uvula	6.60		L	-36	-69	-23
9	< 0.001	76	Precuneus	6.49	19	R	40	-76	39

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10	< 0.001	72	Cerebellum - Culmen	6.35		L	-8	-54	-1
			Lingual Gyrus	5.77	18	L	-18	-54	5
11	< 0.001	125	Inferior Frontal Gyrus	6.33	9	R	53	13	27
12	< 0.001	33	Superior Occipital Gyrus	6.13	19	R	40	-82	24
13	< 0.001	17	Middle Frontal Gyrus	6.02	46	L	-50	28	23
14	< 0.001	20	Middle Frontal Gyrus	5.98	46	R	53	34	24
15	< 0.001	23	Precuneus	5.74	19	L	-28	-72	33
16	0.001	10	Middle Frontal Gyrus	5.58	9	L	-32	43	35
17	< 0.001	16	Angular Gyrus	5.52	39	R	46	-70	29
18	0.003	7	Superior Parietal Lobule	5.45	7	R	36	-63	51
19	0.004	6	Middle Frontal Gyrus	5.03	6	R	32	15	60

Elaboration vs. Access

Cluster Number	Cluster-level pFWE	Cluster Extent (voxels)	Region	Local Z-Score	BA	Side	Talairach Coordinates		
							x	y	z
1	< 0.001	704	Superior Temporal Gyrus	Inf.	39	R	57	-61	25
			Superior Temporal Gyrus	7.16	39	R	46	-53	25
			Inferior Parietal Lobule	7.06	40	R	48	-58	47
2	< 0.001	341	Precuneus	Inf.	7	R	4	-70	44
			Precuneus	6.78	31	L	-2	-65	25
			Posterior Cingulate Gyrus	6.09	31	L	-6	-55	23
3	< 0.001	450	Angular Gyrus	7.63	39	L	-42	-58	38
			Middle Temporal Gyrus	6.79	39	L	-46	-61	29
			Angular Gyrus	5.24	39	L	-53	-64	31
4	< 0.001	804	Precentral Gyrus	7.49	6	R	51	-4	8
			Transverse Temporal Gyrus	7.30	42	R	63	-7	11
			Precentral Gyrus	7.26	4	R	40	-16	34
5	< 0.001	288	Postcentral Gyrus	7.33	43	L	-57	-11	19

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			Precentral Gyrus	5.99	6	L	-44	-14	34
6	< 0.001	37	Middle Frontal Gyrus	7.04	11	R	46	36	-17
7	< 0.001	99	Superior Frontal Gyrus	7.02	8	R	18	47	38
8	< 0.001	87	Inferior Frontal Gyrus	6.84	47	L	-53	29	-5
			Inferior Frontal Gyrus	6.28	47	L	-53	21	-6
9	< 0.001	45	Middle Frontal Gyrus	6.62	9	L	-40	30	26
10	< 0.001	120	Middle Temporal Gyrus	6.61	19	L	-51	-77	15
			Middle Temporal Gyrus	6.36	39	L	-55	-69	20
11	< 0.001	121	Middle Frontal Gyrus	6.55	11	L	-36	56	-13
			Superior Frontal Gyrus	6.29	10	L	-22	56	-11
			Superior Frontal Gyrus	5.88	10	L	-30	60	-10
12	< 0.001	19	Precuneus	6.41	19	R	28	-81	41
13	< 0.001	83	Medial Frontal Gyrus	6.39	10	L	-6	55	12
			Medial Frontal Gyrus	5.51	10	L	-2	57	5
			Anterior Cingulate Gyrus	5.20	32	L	-2	49	7
14	< 0.001	55	Middle Frontal Gyrus	6.35	10	R	36	56	-6
15	< 0.001	24	Medial Frontal Gyrus	6.15	10	L	-6	66	2

Conjunction Analysis - Recall vs. No Memory / Elaboration vs. No Memory

Cluster Number	Cluster-level pFWE	Cluster Extent (voxels)	Region	Local Z-Score	BA	Side	Talairach Coordinates		
							x	y	z
1	< 0.001	41	Precuneus	6.30	7	L	-2	-56	54
2	< 0.001	63	Middle Temporal Gyrus	5.90	39	L	-42	-75	13
			Middle Occipital Gyrus	5.55	19	L	-50	-73	7
3	< 0.001	50	Middle Temporal Gyrus	5.81	19	R	44	-63	14

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4	0.001	10	Middle Frontal Gyrus	5.60	47	L	-44	31	-2
5	0.001	13	Superior Occipital Gyrus	5.57	19	L	-36	-78	32
6	0.001	11	Middle Frontal Gyrus	5.56	46	L	-42	40	24
7	0.002	9	Superior Frontal Gyrus	5.51	11	L	-32	54	-16
8	< 0.001	46	Superior Temporal Gyrus	5.44	38	L	-51	11	-9
9	0.004	6	Middle Cingulate Gyrus	5.42	32	L	-6	32	26
10	0.004	6	Cerebellum - Tuber	5.38		L	-42	-71	-25
11	0.002	8	Superior Parietal Lobule	5.37	7	L	-8	-65	60
12	0.003	7	Cuneus	5.19	19	L	-10	-78	35

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Volumetric gray-matter differences

Cluster Number	Cluster-level pFWE	Cluster Extent (voxels)	Region	Local Z-Score	BA	Side	Talairach Coordinates		
							x	y	z
1	0.026	1396	Lingual Gyrus	3.88	18	L	-14	-73	7
			Middle Temporal Gyrus	3.88	19	L	-32	-48	8
			Cuneus	3.86	17	L	-18	-77	15
			Insula	3.55	13	L	-40	-22	-4
			Posterior Cingulate	3.46	30	L	-30	-63	12
			Posterior Cingulate	3.46	30	L	-22	-48	13
			Caudate Tail	3.30		L	-38	-31	-5
			Middle Temporal Gyrus	3.11	19	L	-32	-60	10
			Superior Temporal Gyrus	2.80	22	L	-46	-10	-6
			Putamen	2.79		L	-32	-23	1
			Superior Temporal Gyrus	2.71	22	L	-59	-27	5
			Posterior Cingulate	2.65	29	L	-12	-48	12
			Posterior Cingulate	2.57	30	L	-20	-62	5
			Fusiform Gyrus	2.49	20	L	-44	-7	-20
			Lingual Gyrus	2.48	17	L	-16	-86	-1
			Middle Temporal Gyrus	2.31	21	L	-46	-3	-15

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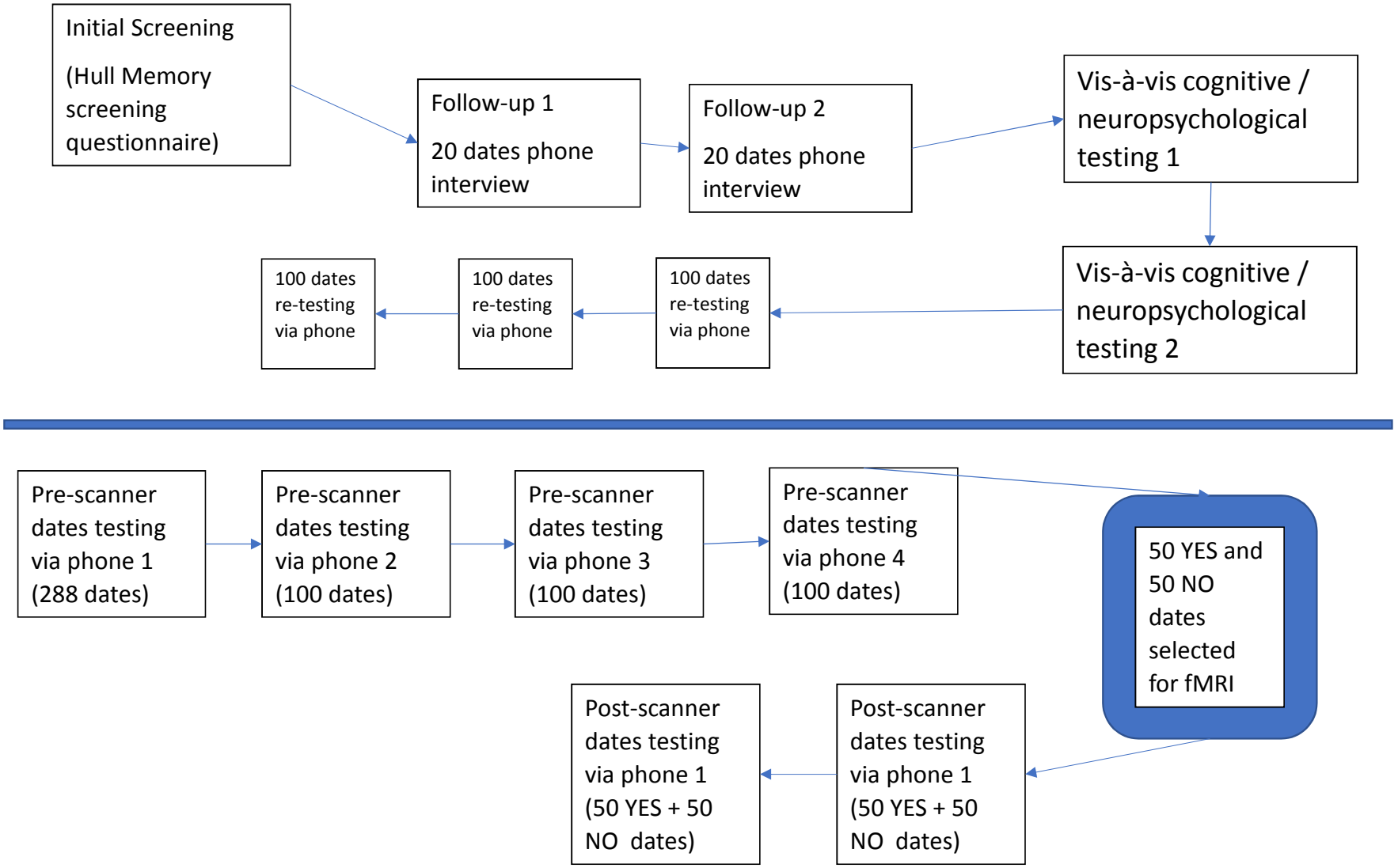
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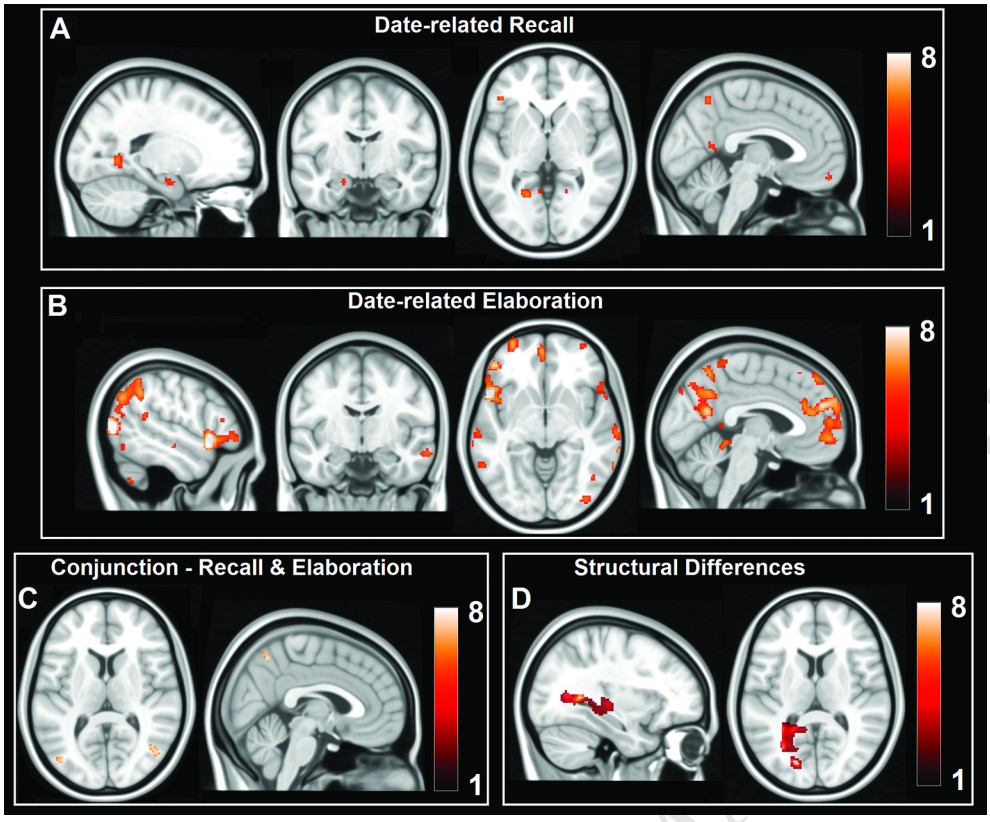
(Hull Memory screening questionnaire)
Follow-up 1
20 dates phone interview
Follow-up 2
20 dates phone interview
Vis-à-vis cognitive / neuropsychological testing 1
Vis-à-vis cognitive / neuropsychological testing 2
100 dates re-testing via phone
100 dates re-testing via phone
100 dates re-testing via phone
Pre-scanner dates testing via phone 1 (288 dates)
Pre-scanner dates testing via phone 2 (100 dates)
Pre-scanner dates testing via phone 3 (100 dates)
Pre-scanner dates testing via phone 4 (100 dates)
50 YES and 50 NO dates selected for fMRI
Post-scanner dates testing via phone 1 (50 YES + 50 NO dates)
Post-scanner dates testing via phone 1 (50 YES + 50 NO dates)



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